In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 12-551V
Filed: March 30, 2016
To be Published

PATRICK J. AGNEW and CONSTANCE M. AGNEW, Parents of R.P.A., a minor,	*	
Petitioners,	*	
v.	*	Flu Mist vaccine ("LAIV"); acute hepatitis; liver failure; liver transplant
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Tatiana Cody, Kelly Marco, Maureen Urbina, Washington, DC, for petitioners.
Alexis B. Babcock, Washington, DC, for respondent.

MILLMAN, Special Master

RULING ON ENTITLEMENT[1]

On August 30, 2012, petitioners filed a petition pro se under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012), alleging that Flu Mist vaccine (a live, attenuated influenza vaccine or "LAIV") which their son R.P.A. received on September 28, 2009 caused him acute hepatitis resulting in liver failure and a liver transplant. Pet., at ¶ 2. On January 14, 2013, petitioners filed a Consent, Approval and Appearance Praecipe to allow law students in the George Washington School of Law Vaccine Injury Clinic to represent them. The initial and subsequent students have ably performed their duties through the hearing on entitlement conducted October 20, 2015, assisted by attorneys Renée J. Gentry and Clifford J. Shoemaker as instructors.

[1] Vaccine Rule 18(b) states that all decisions of the special masters will be made available to the public unless they contain trade secrets or commercial or financial information that is privileged and confidential, or medical or similar information whose disclosure would constitute a clearly unwarranted invasion of privacy. When such a decision is filed, petitioners have 14 days to identify and move to redact such information prior to the document's disclosure. If the special master, upon review, agrees that the identified material fits within the categories listed above, the special master shall redact such material from public access.

Petitioners filed their post-hearing brief on January 28, 2016.

Respondent filed her post-hearing brief on March 14, 2016.

Petitioners filed their reply brief on March 28, 2016.

This case is now ready for decision.

FACTS

R.P.A. was born on March 30, 1999.

On September 28, 2009, he received Flu Mist vaccine. Med. recs. Ex. 1, at 1; Ex. 55, at 1.

On October 13, 2009, R.P.A.'s mother telephoned Dr. Deborah Zinck's pediatric office to report that R.P.A. had stomach aches that started the prior Thursday (October 8, 2009)[2] and had vomiting the prior Friday (October 9, 2009). Med. recs. Ex. 3, at 56. There was a "stomach bug" at school the prior week. Id. R.P.A. was vomiting again that day and had yellow eyes. Id. His temperature was normal. Id.

R.P.A.'s mother brought him to Dr. Zinck's office on October 13, 2009, where Dr. Zinck noted in her record that he had vomited three times, and had abdominal pain, yellow eyes, and a lower oral intake. Id. at 55. She diagnosed R.P.A. with likely viral hepatitis considering his history of sick contacts at school. Id.

On October 15, 2009, R.P.A. went to the Rhode Island Hospital Emergency Department and, from there, was admitted to the hospital. Med. recs. Ex. 37, at 11, 14. The resident Dr. Laura Adams opined that Epstein Barr virus was probably a less likely cause of R.P.A.'s hepatitis because he had no tonsillar erythema or enlargement. Id. at 23. Dr. Martin thought R.P.A. most likely had a non-typeable viral hepatitis, but she would also consider autoimmune hepatitis. Id. A pediatric gastroenterologist Dr. L.M. Haines opined that R.P.A. had hepatitis of unknown etiology. Id. at 25. Dr. Haines' differential diagnosis included infectious, toxic, autoimmune, and neoplastic causes. Id. An ultrasound showed increased periportal echoes and gallbladder wall thickening, both of which were probably secondary to an inflammatory process in the liver, i.e., acute hepatitis. Id. at 51. R.P.A. was discharged on October 15, 2009. He tested negative for adenovirus, parainfluenza I, II, and III, influenza A and B, and respiratory

[2] Although both R.P.A.'s mother and R.P.A. assert in their respective affidavits that onset of R.P.A.'s symptoms was one day after vaccination, the undersigned does not accept that as the onset interval because the medical records depict a 10-day onset and Dr. Bellanti, petitioners' expert, relied in his expert opinion on there being a 10-day onset. Respondent's expert Dr. McGeady also opined the onset was 10 days. The undersigned credits the contemporaneous histories R.P.A.'s mother and R.P.A. gave to medical and hospital personnel over the time interval they gave six years later in their affidavits when their memories may have become muddled over the passage of time.

syncytial virus. Id. at 50.

Two days later, on October 17, 2009, R.P.A. returned to the Rhode Island Hospital Emergency Department because he had vomited with blood four times, and also had jaundice, nausea, dark urine, and abdominal pain. Med. recs. Ex. 33, at 4. He had lymphadenopathy and tachycardia. Id. at 5. He was admitted to the hospital for a gastrointestinal evaluation. Id. at 6. He was transferred to Yale New Haven Hospital on October 20, 2009 with a diagnosis of acute and subacute necrosis of the liver. Id. at 32. Dr. Albert M. Ross wrote the discharge summary for Rhode Island Hospital, stating that R.P.A. was previously healthy, but now presented with jaundice and coffee ground emesis. Id. at 42-43. Initial autoimmune infectious labs had all been normal. Id. at 43. R.P.A.'s discharge diagnosis was acute hepatitis. Id.

On October 21, 2009, Yale doctors listed R.P.A. for a liver transplant. Med. recs. Ex. 7, at 37. Dr. Katherine L. Lord, a resident in the pediatric ICU, on October 21, 2009 assessed R.P.A. with acute liver failure. Id. at 38. She stated the cause was most likely an infectious etiology given the rapidity of the process, but she would also consider an autoimmune process, Wilson's disease,[3] and alpha-1 antitrypsin.[4] Id. A pediatric infectious disease consultation note on October 21, 2009 states that the onset of R.P.A.'s liver illness was October 8, 2009, noting that he had received FluMist on September 28, 2009. Id. at 47. On October 21, 2009, Dr. Sachan Desai noted that there was an unclear etiology of R.P.A.'s acute liver failure in this immunocompetent, previously healthy host. Id. at 55. Because of the rapidity of R.P.A.'s clinical course, some sort of infectious process was likely, but an untypeable hepatitis was possible. Id. A second issue was R.P.A.'s parents' concern that R.P.A.'s prior FluMist vaccination was related to R.P.A.'s subsequent illness. Id. Dr. Desai noted that the package insert for FluMist did not list gastrointestinal adverse effects. Id. He contacted Dr. Zinck, R.P.A.'s pediatrician, who said she would file a VAERS ("Vaccine Adverse Event Reporting System") report and also find out if there had been any reported gastrointestinal side effects following FluMist vaccination. Id. Dr. Elijah E. Paintsil, an infectious disease specialist, posted an addendum saying he agreed with Dr. Desai's note and found it interesting that R.P.A. had no fever, no weight loss, and no night sweats or other constitutional symptoms. Id. A VAERS search for acute liver failure associated with Flu Mist vaccine failed to find any cases. Med. recs. Ex. 15, at 11.

Dr. Paintsil gave approval for the transplant team to go ahead, noting that an infectious disease process in R.P.A.'s liver was very unlikely due to the absence of infectious agents in R.P.A.'s liver. Med. recs. Ex. 14, at 44. On October 26, 2009, R.P.A. had a liver transplant. Med. recs. Ex. 8, at 36; Ex. 10, at 30. Pathology performed on R.P.A.'s removed liver revealed fulminant hepatic necrosis without clear evidence of etiology. Med. recs. Ex. 23, at 4.

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[3] Wilson's disease is "a rare, progressive, autosomal recessive disease due to a defect in metabolism of copper. . . . Liver disease is the usual presenting symptom in children . . . ." Dorland's Illustrated Medical Dictionary 545 (12th ed. 2012) (hereinafter, "Dorland's").

[4] Alpha-1 antitrypsin is "a plasma protein of the serpin group . . . produced primarily in the liver . . . ." Dorland's at 53.

Pathology did not find viral inclusions by light microscopic examination and by electron microscopy. Med. recs. Ex. 15, at 13; Ex. 23, at 5. R.P.A. had a difficult course with his new liver and contracted cytomegalovirus hepatitis. Med. recs. Ex. 20, at 30. No toxicology screen was performed on R.P.A.'s old liver. Med. recs. Ex 29, at 75.

Affidavits

On September 22, 2015, petitioners filed R.P.A.'s affidavit. Ex. 53. He states that, prior to his receipt of FluMist vaccine, he was healthy and active, playing soccer and hockey. Id. at ¶ 2. He asserts that onset of his illness was 24 hours after he received FluMist. Id. at ¶ 3.

Also on September 22, 2015, petitioners filed R.P.A.'s mother's affidavit. Ex. 52. She also asserts that R.P.A.'s symptoms began the day after he received FluMist, with R.P.A.'s school contacting her to tell her that R.P.A. had a stomach ache and headache, and suggesting she take him home. Id. at ¶ 4. The school was concerned R.P.A. had contracted the stomach bug circulating through the school children. Id. Through the week, R.P.A. health continued to deteriorate with absent appetite, nausea, and vomiting. Id.

TESTIMONY

Petitioners' expert, Dr. Joseph A. Bellanti, an immunologist, testified.[5] Tr. at 22. His opinion is that FluMist activated R.P.A.'s immune system which was misdirected into entering his liver. Id. at 28. Processes, including molecular mimicry, innocent bystander injury, and polyclonal expansion of the immune system, caused R.P.A.'s immune system to be not only directed against FluMist vaccine, but also against his liver. Id.

Dr. Bellanti described the immune system as consisting basically of three parts: (1) the innate immune system (nonspecific immunity: phagocytes, inflammation, natural killer cells, the complement system) which is the first line of defense; (2) the adaptive immune system (T-cells, B-cells consisting of five classes of immunoglobulins, Th1, Th2, Th17, Th3, Tr1), which works together with the innate immune system; and (3) immune complex of antigen, antibody, and complement, which promotes injury (the Gell and Coombs reaction types one, two, three, and four, including cytotoxins or antibodies which can kill cells and may have been the mechanism of damage to R.P.A.'s liver). Id. at 33-34. There is a fourth type in the immune system called delayed hypersensitivity which T-cells carry out. Id. at 34. If the immune system eliminates foreignness, the individual returns to health. Id. at 35. If not, there are tissue-damaging effects.

[5] Dr. Bellanti is Director of the International Center for Interdisciplinary Studies of Immunology at Georgetown University, among other posts. Ex. 41, at 1. He is board-certified in allergy and immunology. Id. at 4. He is past president of the American College of Allergy and Immunology. Id. at 6. He is on the editorial board of Annals of Allergy, Asthma & Immunology. Id. He authored or co-authored 266 articles, the most recent of which was in 2013. Id. at 12-28. He wrote or edited 59 books or articles, including the latest edition of his text Immunology IV. Clinical Applications in Health and Disease (4th ed. 2012). Id. at 43-46.

Id.

The FluMist vaccine which R.P.A. received on September 28, 2009 is a cold-adapted vaccine received intranasally. Id. at 37-38. FluMist replicates only at a lower temperature, at 27 or 29 degrees Centigrade, which is the temperature of the nasal cavity. Id. at 38. The virus cannot replicate at a higher temperature. Id. FluMist is a type of subclinical infection. Id. However, it is a subclinical infection usually without symptoms. Id. at 39. R.P.A.'s immune system was misdirected to cause effects against his liver. Id. Within 10 days of vaccination, R.P.A. had abdominal pain, nausea, increasing yellow color of his skin, a rise in enzymes showing destruction of hepatic cells, overwhelming liver failure (hepatitis), and necessitating a liver transplant. Id. at 39-40. R.P.A. received half the liver from a donor cadaver which unfortunately was infected with cytomegalovirus, one of the herpes viruses. Id. at 40. In order for R.P.A. to successfully retain the transplanted liver, he had to take immunosuppressive drugs which permitted the cytomegalovirus to emerge. Id.

Dr. Bellanti called R.P.A.'s post-vaccinal process an autoimmune attack which either molecular mimicry, polyclonal activation, or innocent bystander caused. Id. at 46. When the FluMist replicates in the nasal cavity, cytokines could be produced which could circulate in the blood and injure the liver. Id. at 50. Lymphocytes circulate in the blood and circulate in the liver. Id. at 50. Certain subsets of T-cells that are called cytotoxic cells (CD-8 cells) can be activated. Id. Dr. Bellanti viewed this process as a logical sequence of cause and effect, and stated the 10-day onset interval was the classic period of inducing an immune reaction. Id. at 54. The first time someone receives a vaccine, there is primary induction of the immune system, usually taking seven to 10 days. Id. at 54. This was R.P.A.'s first FluMist vaccination. Id. at 55.

Dr. Bellanti commented on cross-examination that trying to grow FluMist particles in a laboratory would be fruitless because all laboratories (and he has run one) grow viruses at 37 degrees, but one could never detect the temperature-sensitive virus in FluMist at that temperature because it is active only at 26 or 27 degrees Centigrade. Id. at 61. Dr. Bellanti does not believe R.P.A. had gastroenteritis at the time he presented to his doctor because he had no diarrhea or fever. Id. at 62. None of R.P.A.'s doctors linked the FluMist vaccine causally to R.P.A.'s hepatitis. Id. Autoimmune testing as well as viral testing on R.P.A.'s old liver were negative. Id. at 63-64. The transplant team concluded that an infectious cause was unlikely. Id. at 64.

However, Dr. Bellanti stated that immune-activated injury does not require the presence of an infectious agent because it is not the virus damaging the liver; it is the cells that are activated. Id. at 67. There are two methods for cell death: (1) apoptosis, and (2) necrosis. Id. Apoptosis is programmed cell death without inflammation. Id. at 67-68. Necrosis, however, stimulates the inflammatory response. Id. at 68. If necrosis killed R.P.A.'s liver, one would see inflammation. Id. But if the immune system stimulated apoptosis, one would not see inflammation. Id. Therefore, the absence of inflammation in R.P.A.'s old liver does not detract from his having immune-mediated damage of his liver. Id. No toxicology screen was done on R.P.A.'s old liver, but there is no evidence that R.P.A. was exposed to dangerous chemicals at

school or at home which could have damaged his liver. Id. at 69-70.

Respondent's expert, Dr. Stephen J. McGeady, an immunologist, testified.[6] Id. at 85. He does not believe that FluMist vaccine caused R.P.A.'s liver failure. Id. at 89. FluMist vaccine would be active in the upper respiratory tract, the nose, and the throat. Id. at 91. It is designed to induce mucosal immunity. Id. at 92. Doctors looked for metabolic, genetic, infectious, viral, and autoimmune causes of R.P.A.'s hepatitis, but found none. Id. at 92-93. Autoimmune testing included antinuclear antibody ("ANA"), anti-smooth muscle antibody, and anti-microsomal antibodies; all proved negative. Id. at 94-95. R.P.A.'s complement C3 was not particularly elevated, which means he did not have an acute infection or inflammation. Id. at 95. The biopsy of R.P.A.'s old liver did not support an immune, infectious, or viral cause of his liver failure. Id. at 98.

Dr. McGeady disagreed with Dr. Bellanti's analysis of the modes of cell death. Id. at 101. Apoptosis or autophagy without an inflammatory infiltrate is not the result of a pathologic process. Id. This is how the body continually replaces its cells. Id. Dr. McGeady said it was possible for the FluMist to escape from the mucosal immune compartment into the systemic immune compartment, but if it had attacked the liver, we would expect to see something there, but nothing was there. Id. at 103. Immunologically relevant cells were absent from R.P.A.'s liver. Id. at 105. Cytokines are signaling molecules which call in immunologically relevant cells to a site which needs their presence, but that was not seen in R.P.A.'s liver. Id. R.P.A. had a very mild inflammatory periportal infiltrate, but the rest of the liver did not show this and it was completely destroyed. Id.

Dr. McGeady said the architecture of the liver is an arrangement of the cells around little canals which conduct bile, toxins, and other substances out of the liver into the small intestine. Id. The portal system is the aggregate of these little canals. Id. The doctors found a very mild infiltrate around these little canals that are in the globules of the liver. Id. Dr. McGeady is not sure this finding has any specific significance. Id. at 106. Dr. McGeady did not see that there was any search for cytokines in the liver. Id. If FluMist had caused R.P.A.'s liver failure, Dr. McGeady would not expect to see viral cells in his liver because it was not the virus itself, but the misdirection of the immune system that caused the failure. Id. at 109. He would expect the doctors to have found inflammatory mediators such as complement being elevated and the

[6] Dr. McGeady is board-certified in allergy, immunology, with a sub-board in clinical laboratory immunology. Tr. at 85. The sub-board is a special certification given to immunologists who direct clinical laboratories. Id. at 86. The credential is no longer in existence. Id. Dr. McGeady's current practice is limited to pediatrics at the Nemours Foundation in Wilmington, Delaware. Id. at 86-87. He sees a wide range of patients with allergic diseases such as asthma, allergic rhinitis, food allergies, immune deficiencies, and atopic dermatitis. Id. at 87. He sees patients only in Philadelphia at a site adjacent to Thomas Jefferson University Hospital. Id. He has not recently treated patients with hepatitis. Id. When he was in the military in Vietnam for a year, he saw a lot of hepatitis patients. Id. Dr. McGeady was in Vietnam from 1968-69. Ex. B, at 1. He wrote 45 articles, the most recent of which was in 2004. Id. at 2-5. He wrote eight chapters, the latest of which was "Allergy testing in office practice," in 1999. Id. at 12.

definite presence of inflammatory cells. Id. No toxicology screen was performed on R.P.A.'s old liver. Id. at 111. It would be important to know if he had been exposed to some sort of toxin which might explain massive necrosis of his liver without much evidence of an inflammatory process. Id.

Dr. McGeady said there has not been one case of liver failure attributed to FluMist vaccine in the medical literature. Id. at 112. He also said there has not been one case of FluMist causing a general cytotoxic process resulting in liver failure written in the medical literature. Id. Dr. McGeady does not accept that there has been a plausible medical theory connecting FluMist vaccine to R.P.A.'s liver failure. Id. He does not believe that R.P.A. had autoimmune hepatitis. Id. at 113. He would describe R.P.A.'s hepatitis as of indeterminate cause, stating the cause is not ascertainable given the current state of knowledge. Id. at 114. As far as timing is concerned, a primary immune response and the production of antibody have a classic 10-day interval. Id. But there is no evidence that R.P.A. had an anti-liver antibody and the complement does not look as if it were consumed. Id. at 115. Dr. McGeady does not think R.P.A. had an antibody-mediated reaction. Id. He does not think immunofluorescent staining of the resected liver was done or that the doctors looked for anti-liver antibody. Id. The search for other autoantibodies associated with liver failure was negative. Id.

On cross-examination, Dr. McGeady stated that the pathology of R.P.A.'s liver revealed some inflammatory infiltrates around the periportal areas. These infiltrates consisted largely of lymphocytes, which are immune cells that can lead to apoptosis. Id. at 125. This however would account only for some of the cell death in R.P.A.'s liver, not necrosis of his liver. Id. Apoptosis is normal cell death and turnover. Id. at 127. Necrosis is not a normal process. Id. Hepatitis is inflammation of the liver. Id. at 128. He does not think that gentamicin, an antibiotic in FluMist vaccine, caused R.P.A.'s liver failure because the amount of gentamicin is trivial and it was applied topically to his nasal passages. Id. at 130-31.

R.P.A. had high levels of liver enzymes. Id. at 137. Dr. McGeady does not believe that the inflammation of R.P.A.'s periportals could explain the magnitude of the injury to his liver. Id. at 141. The inflammation was minor compared to the necrosis of R.P.A.'s liver which was major. Id. at 142.

On rebuttal, Dr. Bellanti testified that the immune system is complex, consisting of a network of specialized cells that communicate with each other through cytokines, and orchestrate specific types of reactions to foreignness. Id. at 143-44. His opinion is that FluMist vaccine caused immune activation which destroyed R.P.A.'s liver by apoptosis. Id. at 145. Apoptosis does not just cause programmed cell death as a normal function. Id. Apoptosis kills target cells that are virally infected or cancerous. Id. Apoptosis can employ two mechanisms of cellular death of target cells: (1) a natural killer cell directly punches holes in the target cell or (2) a cytotoxic cell CD-8 can use an antibody as a bridge to kill the target cell. Id. at 145, 146. No inflammation is involved. Id. at 148.

Dr. Bellanti stated that the textbook description of autoimmune liver disease is not what

occurred here. Id. at 149. That textbook entity is associated with autoantibodies to smooth muscle, to cytokines, to chromosomes, and to a variety of autoantibodies. Id. He differentiates this textbook process from the autoimmune attack that FluMist vaccine caused here. Id. This inviolved an immune-mediated attack that did not require the presence of anti-smooth muscle, anticytoplasmic components, etc. Id. at 150. Dr. Bellanti termed it a vaccine immune-activated induced reaction to a live attenuated vaccine, generating cell-mediated injury. Id. Dr. Bellanti clarified it as a vaccine-induced, immune directed injury of liver cells, using cellular mechanisms of killing, mainly apoptosis, which is supported by the lack of inflammation in the liver biopsy and the lack of classic markers of autoimmune liver disease. Id. at 151. It is a cell-mediated injury rather than an antibody-mediated injury. Id. at 152. Autoimmune disease can be either cell-mediated or antibody-mediated. Id. The immune system is immensely specific, and certain individuals are susceptible to cell-mediated, autoimmune disease because of genetics. Id. at 153, 160.

Dr. Bellanti said that natural influenza infection can cause liver disease.[7] Id. at 166. Since FluMist is a live attenuated viral vaccine, he said the same mechanisms that lead to liver destruction with natural influenza infection are by analogy the same mechanisms that occur with FluMist. Id. at 166-67. Dr. Bellanti said that although no specific laboratory evidence supports his opinion, using deductive reasoning fits the many observations together. Id. at 167-68. Relying on the Papic article as well as animal experimentation, he said the connection between the flu virus and the liver is related to major histocompatibility complex (MHC) specificity, and the whole genetic control of the immune system. Id. at 168. R.P.A.'s case is rare. Id. The absence of inflammation in R.P.A.'s liver is very significant because, pieced together indirectly, it suggests that the mechanism of immune-mediated injury was apoptotic cell death. Id. at 169.

Dr. McGeady testified on rebuttal. Id. at 175. He said that R.P.A.'s doctors did not look for natural killer cells and cytotoxic cells in R.P.A.'s liver, but they did not see any significant cellular infiltrate in the parenchyma of his liver. Id. at 175-76. They saw lymphocytes in the periportal area. Id. at 176. Dr. Bellanti responded that the presence of inflammatory cells is not required or characteristic of apoptotic cell death which natural killer cells or CD-8 cells mediate. Id. Dr. McGeady responded that the liver was partially destroyed with still viable islands of tissue but no infiltrating cells. Id. at 177. He did not agree with Dr. Bellanti's explanation. Id. Dr. Bellanti concluded by stating that he would relate the molecular mimicry, innocent bystander, and polyclonal activation mechanisms to the cell-mediated process. Id. at 184.

DISCUSSION

To satisfy their burden of proving causation in fact, petitioners must prove by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury;

[7] Dr. Bellanti based this statement on the Papic article, "Liver involvement during the influenza infection: perspective on the 2009 influenza pandemic," by N. Papic, et al., 6 Influenza and Other Respiratory Viruses 3:e2-e5 (2012). Doi:10.1111/j.1750-2659.2011.00287.x., submitted as part of Exhibit 49, but not otherwise demarcated. Tr. at 168.

(2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.'" Althen v. Sec'y of HHS 418 F.3d 1274, 1278 (Fed. Cir. 2005). In Althen, the Federal Circuit quoted its opinion in Grant v. Secretary of Health and Human Services, 956 F.2d 1144, 1148 (Fed. Cir. 1992):

> A persuasive medical theory is demonstrated by "proof of a logical sequence of cause of and effect showing that the vaccination was the reason for the injury [,]" the logical sequence being supported by a "reputable medical or scientific explanation[,]" i.e., "evidence in the form of scientific studies or expert medical testimony[.]"

418 F.3d at 1278.

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, 956 F.2d at 1149. Mere temporal association is not sufficient to prove causation in fact. Id. at 1148.

Petitioners must show not only that but for receiving FluMist vaccine, R.P.A. would not have had hepatitis followed by liver necrosis and liver transplant, but also that FluMist vaccine was a substantial factor in causing R.P.A.'s hepatitis, liver necrosis, and liver transplant. Shyface v. Sec'y of HHS 165 F.3d 1344, 1352 (Fed. Cir. 1999).

Petitioners were unable to give a specific biological mechanism explaining how R.P.A.'s immune response to FluMist vaccine led to hepatitis, liver necrosis, and liver transplant, although their expert Dr. Bellanti proposed the following theories as mechanisms: molecular mimicry, innocent bystander, and polyclonal activation. Petitioners do not have the burden of proving a specific biological mechanism in order to prevail in their case. As the Federal Circuit stated in Knudsen v. Secretary of Health and Human Services, 35 F.3d 543 (Fed. Cir. 1994):

> [T]o require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims. The Vaccine Act established a federal "compensation program" under which awards are to be "made to vaccine-injured persons quickly, easily, and with certainty and generosity." House Report 99-908, supra, at 3, 1986 U.S.C.C.A.N. at 6344. . . .

35 F.3d at 549.

The Federal Circuit stated in Althen, 418 F.3d at 1280, "While this case involves the possible link between [tetanus toxoid] vaccination and central nervous system injury, a sequence hitherto unproven in medicine, the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines

affect the human body." Close calls are to be resolved in favor of petitioners. Capizzano v. Sec'y of HHS, 440 F.3d 1317, at 1327 (Fed. Cir. 2006); Althen, 418 F.3d at 1280.

In addition, the Federal Circuit in Althen stated: "If the Vaccine Act does not require Althen to provide medical documentation of plausibility, then it cannot require her to demonstrate that her specific injury is recognized by said medical documentation of plausibility." 418, F.3d at 1281.

As the Federal Circuit stated in Knudsen, 35 F.3d at 549:

> The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP and other vaccines sometimes destroy the health and lives of certain [vaccinees] while safely immunizing most others. This research is for scientists, engineers, and doctors working in hospitals, laboratories, medical institutes, pharmaceutical companies, and government agencies. The special masters are not 'diagnosing' vaccine-related injuries. The sole issues for the special master are, based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [vaccinee's] injury. . . .

Prong One of Althen

The undersigned is impressed by the considerable expertise of Dr. Bellanti, a still active immunologist with an exhaustive array of responsibilities and medical literature and textbook output. His experience and knowledge in immunology are superior to that of Dr. McGeady who currently functions as a pediatrician. Dr. Bellanti explained that R.P.A.'s liver failure was due to an autoimmune reaction to FluMist vaccine that took the form of a cell-mediated process, initiating apoptosis or cell death that does not involve inflammation. Dr. Bellanti admitted there is no direct proof of this process, but he testified that he and other doctors use deductive reasoning based on their education and experience to reach an understanding, imperfect though it may be, of how the immune system works and how it malfunctions. As the Federal Circuit has said repeatedly, the field of vaccine causation lacks complete and direct proof and must rely on circumstantial evidence. The undersigned follows the Federal Circuit's guidance.

Under prong one of Althen, the undersigned finds that FluMist vaccine can cause an autoimmune reaction by a cell-mediated process leading to hepatitis and liver failure, necessitating a liver transplant. Although rare, even the wild influenza virus can lead to adverse effects in the liver per the Papic article upon which Dr. Bellanti relied. He stated it was reasonable that illnesses that influenza virus in its wild state can cause can also be caused by an attenuated viral vaccine such as FluMist. Petitioners have proved a medical theory showing that FluMist vaccine can cause hepatitis and liver failure, necessitating liver transplantation. Petitioners have satisfied prong one of Althen.

Prong Two of Althen

The preponderance standard requires a petitioner to demonstrate that it is "more likely than not" that the vaccine at issue caused the vaccinee's injury. Moberly v. Sec'y of HHS, 592 F.3d 1315, 1322 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of HHS 931 F.2d 867, 873 (Fed. Cir. 1991). To determine if petitioners have carried their burden, the special master must assess "the record as a whole" and may not make an entitlement decision in their favor based solely on their claims "unsubstantiated by medical records or by medical opinion." 42 U.S.C. § 300aa-13(a)(1). The special master weighs "the persuasiveness of particular evidence . . . [and assess[es] the reliability of testimony, including expert testimony." Moberly, 592 F.3d at 1325.

In this case, none of R.P.A.'s treating doctors opined that the cause of R.P.A.'s hepatitis and liver failure was FluMist vaccine. This, however, does not prevent petitioners from prevailing because they submitted Dr. Bellanti's testimony, which shows the logical sequence of how FluMist vaccine can, and this case did, cause R.P.A.'s hepatitis and its sequelae. The undersigned finds Dr. Bellanti's explanation credible and his vast experience and impressive credentials supportive of finding his opinion credible.

R.P.A.'s case is extraordinarily rare. Dr. Bellanti said that the only explanation he could find for why R.P.A. underwent such a rare and catastrophic process was that he has some unknown genetic susceptibility to the effects of FluMist. Unfortunately, science and medicine have not reached a point where we have complete knowledge of genetic susceptibilities to this kind of reaction. It is unnecessary for the undersigned to hold that R.P.A. has an unknown genetic susceptibility for petitioners to prevail in this case. The undersigned accepts Dr. Bellanti's explanation of the logical sequence of cause and effect of the FluMist vaccine causing R.P.A.'s hepatitis and its sequelae. This proof is paramount. Petitioners need not prove another substantial factor in R.P.A.'s unfortunate illness in order to prevail under the Vaccine Program once the undersigned accepts Dr. Bellanti's expert opinion concerning the vaccine and its effects.

Under prong two of Althen, the undersigned finds that petitioners have proved a logical sequence of cause and effect. While perfectly healthy, R.P.A., after receiving FluMist vaccine, contracted hepatitis with its sequela of liver failure necessitating liver transplantation. Petitioners have satisfied prong two of Althen.

Prong Three of Althen

Ten days after he received FluMist vaccine, R.P.A. was stricken with hepatitis leading to liver failure and liver transplantation. Dr. Bellanti testified that 10 days is an appropriate interval to support vaccine causation. Respondent's expert Dr. McGeady admitted 10 days is an appropriate time interval to signify causation of an autoimmune disease. However, Dr. McGeady qualified his answer by stating he did not accept Dr. Bellanti's theory of causation. Dr. McGeady's caveat does not vitiate his admission that, were he to accept Dr. Bellanti's

theory, a 10-day onset would be appropriate for vaccine causation.

Under prong three of Althen, the undersigned finds that the 10-day interval between R.P.A.'s receipt of FluMist vaccine and the onset of his autoimmune hepatitis is appropriate for causation from the vaccine, according to both experts. Petitioners have satisfied prong three of Althen.

The undersigned holds that petitioners are entitled to compensation.

CONCLUSION

Petitioners have prevailed on the issue of entitlement. The undersigned will schedule a telephonic status conference soon to discuss resolution of damages.

IT IS SO ORDERED.

Dated: March 30, 2016

/s/ Laura D. Millman
Laura D. Millman
Special Master